

REPELLENTS AND THE MILITARY: OUR FIRST LINE OF DEFENSE

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HISTORY AND DEVELOPMENT

The U.S. military has been a major customer for the development of repellents since World War II. During the war, the U.S. Department of Agriculture was tasked with finding both topical (applied to the skin) and clothing repellents for forces in the field. The urgency of this task was based on the lack of effective drugs for prevention of malaria and the total absence of drugs for treatment of louse-borne typhus (epidemic typhus) and chigger-borne typhus (scrub typhus). Among the early repellents developed and recommended for military use were dimethyl phthalate, indalone, and ethyl hexanediol. A mixture of these chemicals known as 6–2–2 (6 parts of dimethyl phthalate, 2 parts of ethyl hexanediol, and 2 parts of indalone) became the standard military repellent in the latter part of World War II (Travis et al. 1946). The next best repellent combination, known as M-2020 (40% dimethyl phthalate, 30% dimethyl carbate, 30% ethyl hexanediol), was adopted as the military standard topical repellent in the early 1950s (U.S. Department of Agriculture Circular # 977, 1955).

In 1951, a new repellent mixture, M-1960, was adopted as the standard clothing repellent for the military (Gilbert and Gouck 1953). M-1960 contained 30% 2-butyl-2-ethyl-1,3-propanediol for protection against mosquitoes and biting flies, 30% N-butylacetanilide for ticks, 30% benzylbenzoate for chigger mites and fleas, and 10% Tween 80 as an emulsifier. This repellent was applied to clothing in the Pacific Theater in a successful attempt to blunt the devastating effects of scrub (chigger-borne) typhus. Unfortunately, this mixture caused skin irritation and its use had to be discontinued after the war. A new and effective clothing repellent was not fielded until 1991, when the synthetic pyrethroid, permethrin, came into use and was adopted as the standard military clothing repellent (AFPMB Technical Guide 36, 1996). Today, military personnel use permethrin to repel and kill arthropods that land on many kinds of treated surfaces, including field uniforms, tents, bed nets, and helmet covers.

DEET

The familiar active ingredient, N,N-diethyl-3-methyl-benzamide (DEET), was first marketed commercially in 1956. It was adopted in a 75% ethanol formulation by the military as the standard topical insect repellent in 1957. Although an effective repellent, it had a number of drawbacks. The application lasted for only 1 or 2 h in warm and humid conditions, felt very oily on the skin, had an

objectionable odor, and was a strong plasticizer (AFPMB Technical Guide 36, 1996). As a result, troops did not like to use it and most did not use it. Over 62% of 1,500 soldiers who responded to a questionnaire urged the Army to get a better repellent (Hooper and Wirtz 1983). In 2001, the Armed Forces Pest Management Board cancelled the National Stock Number (NSN 6840-00-753-4963) for 75% DEET. In 1990, the standard military topical arthropod repellent was changed to a sustained-release, polymer formulation, known as the extended duration topical insect and arthropod repellent (EDTIAR). This product was developed by the Department of Defense (DoD) in collaboration with the 3M Corporation. It contains 33% DEET and provides 6 h of at least 95% protection against a variety of mosquito species in a tropical environment; 10 h in a hot, dry environment; and 12 h in a forested/wet environment (Gupta and Rutledge 1989).

ARMED FORCES PEST MANAGEMENT BOARD TECHNICAL GUIDE

One of the excellent developments for personal protection of troops was not a repellent, but a manual on how to prevent insect bites. This manual is produced by the Armed Forces Pest Management Board as Technical Guide (TG) 36, "Personal Protective Measures Against Insects and Other Arthropods of Military Significance," which can be downloaded from the web site <http://www.afpmb.org>. It is a comprehensive guide for military personnel on all aspects of personal protection, from arthropod avoidance to clothing treatment. The basic DoD insect repellent system for personal protection consists of the application of EDTIAR to exposed skin, the permethrin clothing treatment, and proper wear of the uniform (mainly that the sleeves are kept down and trousers bloused into boots). The manual also includes a set of briefing slides for instruction of military personnel.

INSECT REPELLENT SCIENCE AND TECHNOLOGY OBJECTIVE

In 1999, the Department of the Army approved a science and technology objective (STO) for development of a new topical standard military insect repellent. The objective of the STO was to develop a new repellent that is user friendly, accepted by each military member, and that maintains the effectiveness of the EDTIAR. The STO took advantage of recent progress in discovery of active ingredients that are more effective than DEET,

offering the possibility of reducing the percentage of the active ingredient. The DoD Repellent Program also used recent formulation technology to produce a product that has the consistency and feel of hand lotion, in contrast with the current EDTIAR, which is greasy, sticky, and as thick as toothpaste. The STO was completed successfully in 2005, producing 3 candidate active ingredients in new formulations that are easier to use than the EDTIAR.

The military has a long history of in-house research on repellents. Some of this work has been directed at finding out why soldiers do not like to apply repellents. These sorts of studies have been valuable in providing direction to the STO and other research efforts. The military has also been involved in the development of new active ingredients in collaboration with the U.S. Department of Agriculture's (USDA) Chemicals Affecting Insect Behavior Laboratory in Beltsville, MD. Improvement in formulation was the basis for fielding the EDTIAR and the military continues to have an interest in formulation technology that produces a product that is easier to apply and more resistant to wetting and abrasion. To support this work, the military has developed new methods for repellent testing that expand on the excellent work at USDA. These methods include new statistics, *in vitro* testing (without the use of animal or human models) (Klun et al. 2005), new laboratory human repellent tests using a module for quantitative evaluation of repellent efficacy (Klun and Debboun 2000), and computer modeling of repellent activity (Ma et al. 1999).

The bottom line in the evaluation of any repellent test is how it performs in the field. With 5 overseas laboratories (Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand; United States Army Medical Research Unit—Kenya, Nairobi, Kenya; Naval Medical Research Unit-3, Cairo, Egypt; Naval Medical Research Center Detachment, Lima, Peru; and Naval Medical Research Unit 2, Jakarta, Indonesia) and collaboration with the Australian Army Malaria Institute, the U.S. military is in an excellent position to test repellents against vectors of many diseases.

CAMOUFLAGE FACE-PAINT INSECT REPELLENT

In order to provide soldiers and marines in a tactical environment with more convenient protection from biting arthropods, the Walter Reed Army Institute of Research (WRAIR) Repellent Program collaborated with Amon Re, Inc., to develop a new, improved formulation of camouflage face paint without insect repellent and a combined camouflage face-paint insect repellent (CFPIR) formulation containing 30% DEET. In 1999, the new combined CFPIR formulation containing 30% DEET with 4 colors (loam, green, sand, and white) was tested for

soldier user acceptability with 300 infantry soldiers during a joint multinational military training exercise, Operation Cobra Gold 1999 at Nakhon Ratchasima (Korat), Thailand. Results of the study showed that the new formulation of CFPIR with 30% DEET was accepted and liked by the soldiers, rated higher than the old formulation of camouflage face paint and was recommended to be used by other soldiers (Debboun et al. 2000).

A clinical efficacy trial at the WRAIR in October 2000 demonstrated that the CFPIR formulated with 30% DEET for all 5 colors (black, green, loam, sand, and white) met and exceeded the minimum repellency requirement stated in the Army's approved Operational Requirement Document (ORD) for a minimum of 8 h of protection against biting arthropods. The product was evaluated in an environmental chamber at the Natick Soldier Center in May 2001, demonstrating that the new formulation of CFPIR with 30% DEET spread easily and evenly on human skin at a temperature as low as 20°F and as high as 120°F.

In July 2001, another user acceptability evaluation of the new formulations was performed by 349 U.S. Army infantry soldiers in the Republic of Korea. Results showed that the new CFP formulation with 30% DEET was more acceptable to soldiers than the CFP formulation without DEET (70.5% versus 52.9%, respectively). The new combined CFPIR formulation with 30% DEET will offer significant operational advantages: protection from pathogen-transmitting arthropods, elimination of the need to carry separate insect repellent and camouflage face paint, and reduction in the time required to apply repellent and camouflage face paint separately.

Recently, the Armed Forces Pest Management Board Executive Council approved the assignment of a national stock number (NSN) for the new camouflage face paint with and without DEET insect repellent, resulting in the Defense Supply Center—Richmond assigning the following NSNs: 6840-01-493-7334 for camouflage face paint with 30% DEET and 6850-01-493-7309 for camouflage face paint without 30% DEET.

NEWLY MARKETED REPELLENT ACTIVE INGREDIENTS

For many years, DEET appeared to be much more effective than any other active ingredient available for a topical repellent. Recently, good alternative chemicals (i.e., KBR 3023, IR3535, and p-methane diol) have come on the market in various formulations. Each of these new ingredients have some advantages over DEET and their efficacy appears to be good based on laboratory and field studies. Other active ingredients, like methylated soybean oil, may eventually prove to be just as effective. The military has taken the official position that the standard military topical repellent is

preferred over any other product (AFPMB TG 36). Part of the motivation for this position is that those charged with making recommendations can have confidence in the safety and efficacy of their recommendation if the product is well known. Despite recommendations from military authorities or informed professionals, individual soldiers will often use products that they perceive as safer, easier, or more effective. Considering the low rates of acceptance of the standard military repellent, it is probably better for soldiers to have more choices and adapt their use of repellents to their individual needs. As long as the active ingredient of the product is effective against the particular arthropod of concern, greater use of repellent is likely to reduce the likelihood of pathogen transmission.

The disadvantage and advantage of repellents is the same: individual soldiers can apply the product at any time it is necessary. The disadvantage is that repellents require active participation by individuals. The advantage is that the repellents can be applied anywhere with no prior preparation. Considering the challenges of vaccinating large numbers of troops (e.g., Dyer 2004), repellents are likely to have a role in protection from vector-borne diseases for a long time to come, regardless of other technological developments. The combination of vector control and personal protection can be surprisingly effective in protecting military personnel when they are deployed overseas anywhere in the world (Strickman et al. 2001).

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